

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (previously presented): A cytochrome C-reporter fusion protein construct comprising:

- (a) a modified cytochrome C protein or any functional analogue thereof derived from wild type cytochrome C; and
- (b) a reporter, wherein said modified cytochrome C targets the mitochondria and has a reduced ability to induce apoptosis in a living cell.

Claim 2 (previously presented): The fusion construct of claim 1, wherein said modified cytochrome C binds apoptosis protease activation factor-1 (Apaf-1) at least ten times less than wild type cytochrome C.

Claim 3 (previously presented): The fusion construct of claim 1, wherein said modified cytochrome C binds apoptosis protease activation factor-1 (Apaf-1) at least 100 times less than wild type cytochrome C.

Claim 4 (previously presented): The fusion construct of claim 1, wherein said modified cytochrome C binds apoptosis protease activation factor-1 (Apaf-1) at least 1000 times less than wild type cytochrome C.

Claim 5 (previously presented): The fusion construct of claim 1, wherein at least one of the amino acids of said modified cytochrome C at positions 4, 7, 8, 25, 39, 62, 63, 64, 65 and 72 has been mutated relative to the wild type cytochrome C.

Claim 6 (previously presented): The fusion construct of claim 5, wherein said modified cytochrome C has an amino acid substitution or substitutions selected from the group consisting of K4E, K72A, K72L, K72R, K72G, K72X, E62N, K7E-K8E, K25P-K39H, K7A-E62N-K25P, K7A-E62N-K39H, K7E-K8E-E62N, K7A-K25P-E62N, K7A-E62N-K25P-K39H, E62N-T63N-L64M-M65S, K7E-K8E-E62N-K25P-K39H, K7E-K8E-K25P-E62N-T63N-L64M-M65S, K7E-K8E-K39H-E62N-T63N-L64M-M65S and K7E-K8E-K25P-K39H-E62N-T63N-L64M-M65S.

Claim 7 (withdrawn): The fusion construct of claim 6, wherein said modified cytochrome C comprises the amino acid substitutions selected from the group consisting of K7E-K8E-E62N-K25P-K39H, K7E-K8E-K25P-E62N-T63N-L64M-M65S, K7E-K8E-K39H-E62N-T63N-L64M-M65S and K7E-K8E-K25P-K39H-E62N-T63N-L64M-M65S.

Claim 8 (previously presented): The fusion construct of claim 6, wherein said modified cytochrome C comprises the amino acid substitution selected from the group consisting of K72A, K72L, K72R, K72G and K72X, wherein X represents trimethylation.

Claim 9 (previously presented): The fusion construct of claim 6, wherein said modified cytochrome C comprises the amino acid substitution K72A or K72L.

Claim 10 (withdrawn): The fusion construct of claim 6, wherein said modified cytochrome C comprises the amino acid substitution K4E.

Claim 11 (previously presented): The fusion construct of claim 1, wherein said reporter is a fluorescent protein or a functional analogue thereof.

Claim 12 (original): The fusion construct of claim 11, wherein said fluorescent protein is selected from the group consisting of Green Fluorescent Protein (GFP), Yellow Fluorescent Protein (YFP), Blue Fluorescent Protein (BFP), Cyan Fluorescent Protein (CFP), Red Fluorescent Protein (RFP), Enhanced Green Fluorescent Protein (EGFP) and Emerald.

Claim 13 (previously presented): The fusion construct of claim 11, wherein said fluorescent protein is Enhanced Green Fluorescent Protein or Emerald.

Claim 14 (previously presented): The fusion construct of claim 11, wherein said GFP comprises:

- i) an amino acid substitution at position F64L;
- ii) an amino acid substitution at position S175G; and
- iii) an amino acid substitution at position E222G.

Claim 15 (previously presented): The fusion construct of claim 1 selected from the group consisting of SEQ ID NO: 4 and SEQ ID NO: 6.

Claim 16 (previously presented): The fusion construct of claim 1, wherein the reporter is localisable by a detectable luminescent, fluorescent or radio-active moiety.

Claim 17 (previously presented): The fusion construct of claim 16, wherein the reporter comprises an immunogenic motif.

Claim 18 (previously presented): The fusion construct of claim 16, wherein the reporter comprises a cysteine-rich motif.

Claim 19 (previously presented): The fusion construct of claim 16, wherein said detectable moiety comprises a bi- arsenical compound.

Claim 20 (previously presented): The fusion construct of claim 16, wherein said moiety comprises an antibody.

Claim 21 (previously presented): A nucleotide sequence encoding the fusion construct of claim 1.

Claim 22 (previously presented): A nucleotide sequence selected from the group consisting of SEQ ID NO: 3 and SEQ ID NO 5.

Claim 23 (previously presented): A nucleic acid construct comprising a suitable control region and the nucleotide sequence of claim 21, said sequence being under the control of said control region.

Claim 24 (previously presented): The nucleic acid construct of claim 23 being under the control of a promoter selected from the group consisting of native cytochrome C promoter, mammalian constitutive promoter, mammalian regulatory promoter, human ubiquitin C promoter, viral promoter, SV40 promoter, CMV promoter, yeast promoter, filamentous fungal promoter and bacterial promoter.

Claim 25 (previously presented): The nucleic acid construct of claim 24, wherein said viral promoter is the CMV or the SV40 promoter.

Claim 26 (previously presented): The nucleic acid construct of claim 24, wherein the promoter is the human ubiquitin C promoter.

Claim 27 (previously presented): A replicable vector comprising the nucleic acid construct of claim 23.

Claim 28 (original): The replicable vector of claim 27, wherein said vector is a plasmid vector.

Claim 29 (original): The replicable vector of claim 27, wherein the vector is a viral vector.

Claim 30 (original): The replicable vector of claim 29, wherein said viral vector is selected from the group consisting of cytomegalovirus, Herpes simplex virus, Epstein-Barr virus, Simian virus 40, Bovine papillomavirus, Adeno-associated virus, Adenovirus, Vaccinia virus and Baculovirus vector.

Claim 31 (previously presented): A host cell stably transformed with the nucleic acid construct of claim 23.

Claim 32 (previously presented): A host cell transiently transformed with the nucleic acid construct of claim 23.

Claim 33 (previously presented): The host cell of claim 31 selected from the group consisting of plant, insect, nematode, bird, fish and mammalian cell.

Claim 34 (original): The host cell of claim 33, wherein said mammalian cell is a human cell.

Claim 35 (original): The host cell of claim 34, wherein said human cell is selected from the group consisting of Hek, HeLa, U2OS and MCF-7.

Claim 36 (original): The host cell of claim 35, wherein said Hek cell is Hek293.

Claim 37 (previously presented): The host cell of claim 31 capable of expressing the fusion protein of claim 1.

Claim 38 (previously presented): A method for detecting apoptosis in a living cell comprising the steps of:

- i) culturing a cell transformed to over-express the fusion construct of claim 1; and
  - ii) determining the localisation of the fusion construct within the cell with time;
- wherein a change in localisation of the fusion construct within the cell is indicative of apoptosis.

Claim 39 (withdrawn): A method for measuring the effect that an agent has upon modulating apoptosis in a living cell comprising the steps of:

- i) culturing a cell transformed to over-express the fusion construct of claim 1;
- ii) determining the localisation of said construct within the cell;
- iii) treating the cell with said agent and determining the localisation of the construct within the cell;

wherein any difference in the localisation of the construct within the cell relative to control cells untreated with the agent is indicative of the effect that the agent has upon modulating apoptosis.

Claim 40 (withdrawn): A method for measuring the effect an agent has upon modulating apoptosis in a living cell comprising the steps of:

- i) culturing a first cell and a second cell which both over-express the fusion construct of claim 1;
- ii) treating said first cell with said agent and determining the localisation of said construct within the first cell;
- iii) determining the localisation of the construct within said second cell which has not been treated with the agent;

wherein any difference in the localisation of the construct within the first cell and second cell is indicative of the effect that the agent has upon modulating apoptosis.



Claim 41 (previously presented): A method for measuring the effect an agent has upon modulating apoptosis in a living cell comprising the steps of:

- i) culturing a cell transformed to over-express the fusion construct of claim 1;
- ii) treating said cell with said agent and determining the localisation of the construct within the cell;
- iii) comparing the localisation of the construct in the presence of the agent with a known value for the localisation of the construct in the absence of the agent;

wherein any difference in the localisation of the construct within the cell in the presence of the agent and said known value in the absence of the agent is indicative of the effect that the agent has upon modulating apoptosis.

Claim 42 (withdrawn): The method of claim 41, wherein the known value is stored on a database.

Claim 43 (withdrawn): The method of claim 38-41, wherein the localisation of said fusion construct is measured by its luminescence, fluorescence or radioactive properties.

Claim 44 (withdrawn): The method of claim 39-41, wherein said agent induces apoptosis.

Claim 45 (withdrawn): The method of claim 39-41, wherein the agent inhibits apoptosis.

Claim 46 (withdrawn): The method of claim 38-41, wherein the localisation of the protein fusion is determined following fixation of the cells.

Claim 47 (withdrawn): The method of claim 38-41, where the agent is a chemical, physical or biological agent.